CASE REPORT

Neuro-Sweet Disease Causing Orbital Inflammation

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ABSTRACT

Neuro-Sweet disease is a rare condition causing encephalitis or meningitis in addition to the erythematous skin plaques of Sweet syndrome. Neuro-Sweet disease has been associated with several ocular manifestations, including ocular movement disorders, episcleritis, conjunctivitis, uveitis, and optic disc oedema. The author reports a patient with orbital inflammation, cranial neuropathies, and a skin rash in the setting of myelodysplastic syndrome. Biopsy of her skin lesion confirmed the diagnosis of neuro-Sweet disease. To the author's knowledge, this is the first reported case of neuro-Sweet disease causing orbital inflammation. Her ocular inflammation resolved with the use of systemic corticosteroid treatment.

Keywords: Neuro-Sweet disease, orbital cellulitis, orbital inflammation, Sweet syndrome

INTRODUCTION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a condition that causes fever, neutrophilia, and erythematous skin plaques, whereas neuro-Sweet disease is an entity first described in 1999 that causes neurologic manifestations in addition to the findings of Sweet syndrome.¹ Neuro-Sweet disease has been reported to cause ocular manifestations such as episcleritis, conjunctivitis, uveitis, and optic disc oedema.^{2,3} I report a case of neuro-Sweet disease causing bilateral orbital inflammation mimicking orbital cellulitis.

CASE REPORT

A 56-year-old female was transferred to the university medical centre from another hospital because of altered mental status, fevers, and possible myelodysplastic syndrome. Upon admission, the ophthalmology service was consulted to evaluate her recent increased intraocular pressures. The patient had also been experiencing alternating proptosis and intermittent diplopia for the past 3 weeks. For 1 week, she had also been experiencing right upper eyelid ptosis and

right lower motor neuron seventh nerve palsy, as well as a pressure sensation of the right eye. An ophthalmologist had evaluated her prior to transfer, noted an intraocular pressure in the 30s, and treated her with intravenous mannitol, which relieved the patient's pressure sensation. She had a history of known open-angle glaucoma, and her medication regimen had also been changed to include timolol, bimatoprost, and brimonidine in both eyes.

Her systemic symptoms had begun 1 month before, when she underwent a dental procedure resulting in a chronically draining dental abscess. One week after the procedure, she developed headache, neck pain, and a skin rash. She was admitted to a local hospital, and magnetic resonance imaging (MRI) showed an epidural abscess of the cervical spine, which was treated with ceftriaxone and vancomycin. Due to leukocytosis, she also underwent bone marrow biopsy, showing 13% blasts. She was discharged home and continued to receive antibiotics, but was readmitted due to recurrence of her fever. Her treatment was changed to include vancomycin, ceftazidime, and metronidazole. Repeat MRI did not show an epidural abscess. However, during this hospitalisation, she developed a right lower motor neuron seventh nerve palsy. Maxillofacial computed tomography was done

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and showed no abnormalities along the course of cranial nerve VII. MRI of the brain was done and was reportedly unremarkable. Her white blood cell count then increased to 60,000/ μ L, and for this reason she was transferred to the haematology-oncology service at the university medical centre for evaluation of suspected haematologic malignancy. Her past medical history was significant for hypothyroidism and moderate obesity. Her past family and social history were unremarkable.

On bedside ophthalmologic examination, her near visual acuity with correction was 20/100 OD and 20/60 OS. Her intraocular pressure by Tonopen was 23 mm Hg OD and 15 mm Hg OS. Pupils were 3 mm in the dark and 2 mm in the light, and there was a relative afferent pupillary defect (RAPD) OD. Confrontation visual field was full in each eye. Her ocular motility revealed complete ophthalmoplegia OD and was full OS. She also had diminished sensation to pin-prick and light touch on the right side in the V1 and V2 distribution, as well as a right lower motor neuron cranial nerve VII palsy. Her external examination was significant for proptosis of both eyes, right greater than left. She had complete ptosis of the right upper eyelid, with moderate eyelid oedema, but had normal lids on the left. Anterior segment examination OD was significant for 4+ diffuse conjunctival injection that partially blanched with application of phenylephrine. The remainder of her anterior segment examination was normal. Her dilated fundus examination revealed a cup-to-disc ratio of 0.5 in each eye without optic disc oedema or pallor. She had normal macula, vessels, and periphery OU. Her ocular examination findings were felt to be consistent with orbital cellulitis OD. Treatment was continued with broad-spectrum antibiotics, and neuro-imaging was ordered.

MRI of the brain and orbits with fat suppression and with and without contrast was performed and showed diffuse leptomeningeal and pachymeningeal enhancement involving supratentorial and infratentorial structures, orbital fat, as well as optic nerve sheaths bilaterally (Figures 1, 2). There was also prominent cerebrospinal fluid (CSF) space along the optic nerve sheath, suggesting increased intracranial pressure. There were no orbital masses or subperiosteal orbital abscesses. Finally, there was diffuse opacification of the mastoid air cells and the left petrous apex raising concern of infection. She had no intracranial tumour, empty sella, or hydrocephalus.

Because of her MRI findings, she underwent a lumbar puncture, which was significant for an increased opening pressure of 31 cm of H₂O. CSF glucose was normal at 61 mg/dL, protein was elevated at 67 mg/dL, red blood cell count was 3/ μ L, and white blood cell count was 4/ μ L (73% neutrophils, 16% lymphocytes, 11% macrophages). CSF cultures and cytology were negative. The CSF was also negative for

FIGURE 1 Magnetic resonance imaging of orbits, coronal post-contrast T1, showing mild bilateral orbital fat enhancement ("dirty fat" sign) and prominent cerebrospinal fluid space along the optic nerve sheaths.

FIGURE 2 Magnetic resonance imaging of orbits, axial post-contrast T1, showing proptosis, right eye > left eye, and diffuse leptomeningeal and pachymeningeal enhancement.

anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, and rheumatoid factor. Otolaryngologic examination showed no clinical signs of sinus infection. Dental evaluation resulted in the extraction of 3 teeth due to infection. She treated with broad-spectrum antibiotic and antiviral treatment without any improvement of her orbital cellulitis or cranial neuropathies over the next week, suggesting that the inflammation was not infectious in aetiology. For this reason, the addition of systemic steroid to manage her orbital inflammation was recommended. At this time, she was also diagnosed with myelodysplastic syndrome and started on chemotherapy (cytarabine, daunorubicin, and pravastatin), as well as a 5-day intravenous course of methylprednisolone 100 mg daily. Her cranial neuropathies were attributed to

infiltrative disease and increased intracranial pressure. Within a few days, her proptosis and conjunctival injection completely resolved. Her vision could not be assessed accurately due to her mental status. However, her ocular motility improved, although she continued to have –2 restriction of abduction, –1 restriction of adduction, supraduction, and infraduction OD. She continued to have an RAPD OD and right upper lid ptosis.

Two weeks later, the patient developed similar symptoms in her fellow eye, with mild left upper lid ptosis, chemosis, and conjunctival injection OS. She also developed –2 restriction of abduction, –1 restriction of adduction, supraduction, and infraduction. At this time, she developed a skin rash with macules and patches over her entire body. A skin biopsy from her leg was performed by the dermatology department, showing extensive erythrocyte extravasation with a mixed cellular infiltrate, many of which had an immature cytologic appearance, but with some mature neutrophils. No organisms were identified. Her skin biopsy was most consistent with Sweet syndrome. Given her associated neurologic and ophthalmologic findings, she was felt to have neuro-Sweet disease with associated orbital inflammation. She was restarted on intravenous methylprednisolone with resolution of her symptoms. She was transitioned to prednisone, which was tapered slowly over several months; however, 10 months later, she had a recurrence of neuro-Sweet disease, with bilateral upper and lower lid oedema and erythema, right peripheral seventh nerve palsy, right conjunctival injection, and right eye pain with movement. She was treated with a pulse of high-dose methylprednisolone, with good response over 3 days and was transitioned back to a slow prednisone taper. She was also started on dapson.

Despite a peripheral blood stem cell transplant and treatment with azacitidine, she experienced a relapse of her myelodysplastic syndrome. The relapse was treated with donor lymphocyte infusion, but unfortunately, she succumbed to her disease and passed away.

DISCUSSION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is an inflammatory disorder that causes fever, neutrophilia, and erythematous skin plaques, with skin biopsies demonstrating dermal infiltration with neutrophils in the absence of vasculitis.⁴ This inflammation can also occur in other organs, including the eyes, lungs, liver, kidneys, gastrointestinal tract, bone marrow, spleen, and muscle.^{2,5} Sweet syndrome can be idiopathic, associated with upper respiratory tract or gastrointestinal infection, inflammatory bowel disease, pregnancy,

malignancy, or drug-induced (most commonly due to granulocyte colony stimulating factor). The syndrome responds well to systemic corticosteroid treatment.⁶

Ocular inflammation occurs in approximately one third of patients with Sweet syndrome. Although the most common ocular manifestations are conjunctivitis or episcleritis, many other types of ocular inflammation have been described, such as scleritis, limbal nodules, peripheral ulcerative keratitis, uveitis, and choroiditis.^{7–12} There have also been two reports of Sweet syndrome causing orbital cellulitis.^{13,14}

The pathologic findings of the conjunctiva in patients with Sweet syndrome are similar to the skin findings, with neutrophilic infiltration and oedema in the absence of vasculitis.^{9–11}

Neuro-Sweet disease is a more recently described entity in which encephalitis or meningitis occurs in addition to classic skin findings of Sweet syndrome. Commonly, neuro-Sweet disease causes corticosteroid-responsive, recurrent encephalitis or meningitis accompanied by fever greater than 38°C and erythematous skin plaques or nodules with neutrophilic infiltration of the dermis. However, there is an absence of cutaneous vasculitis and thrombosis, which distinguishes it from neuro-Behçet disease. There is often an association with human leukocyte antigens HLA-Cw1 and HLA-B54 but not with HLA-B51.²

Neuro-Sweet disease has been described to have several ocular manifestations, including ocular movement disorders, episcleritis, conjunctivitis, uveitis, and optic disc oedema^{2,3}; however, to my knowledge, this is the first reported case of neuro-Sweet disease causing orbital inflammation. This patient had myelodysplastic syndrome, and there is a suggestion that Sweet syndrome secondary to myelodysplastic syndrome can cause more atypical and severe skin, mucous membrane, and ocular lesions.⁹

Although neuro-Sweet disease responds well to systemic corticosteroids, it can recur after steroid taper, as with our patient. One case report highlights the successful use of dapson in the treatment of steroid-dependent neuro-Sweet disease.¹⁵ Although our patient was started on dapson, she passed away from her myelodysplastic syndrome before the effects of the dapson could be determined.

Though rare, neuro-Sweet disease can cause ocular manifestations, and as this case highlights, the manifestations may not be limited to the eye itself but can also involve the orbit and mimic orbital cellulitis.

Consent information: Unable to obtain patient consent for this case report as the patient is now deceased. However, care has been taken to protect the patient's anonymity; specifically, there are no recognizable photos or videos of the patient included with this report.

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